

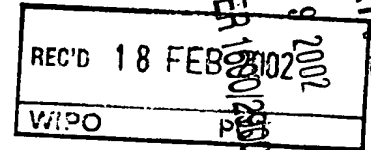
09/868,419

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 23254-04		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/08353	International filing date (day/month/year) 30 March 2000 (30.03.2000)	Priority date (day/month/year) 30 March 1999 (30.03.1999)	
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/03; A61K 35/00, 48/00. and US Cl.: 514/44; 424/93.1, 93.2; 435/320.1.			
Applicant RAN KORNOWSKI			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 30 October 2000		Date of completion of this report 16 October 2001	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer Eleanor Sorbello Telephone No. 703-308-0196	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/08353

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
 pages 1-30 _____ as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____.
- ☒ the claims:
 pages 31-40 _____, as originally filed
 pages NONE _____, as amended (together with any statement) under Article 19
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____.
- ☐ the drawings:
 pages 1-2 _____, as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____.
- ☐ the sequence listing part of the description:
 pages NONE _____, as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/08353

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>1-102</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-102</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-102</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-102 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method for enhancing blood vessel formation by the administration of autologous bone marrow.

----- NEW CITATIONS -----

Isner, Jeffrey M. et al. "Angiogenesis and vasculogenesis as therapeutic strategies for postnatal neovascularization", The Journal of Clinical Investigation, May 1999, vol. 103, No: 9, pages 1231-1236, see page 1234, col. 1, paragraph 2.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/08353

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 8, 10, 49, 66 and 83 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 8 and 10 are indefinite for the following reason(s):

Claims 10, 14-17, 28, 29, 32-35, 45, 46, 49, 62, 63, 66-68, 79, 80, 83, 85 and 86 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims recite the term "gene", in the context of administration of a gene in combination with bone marrow transplantation, without adequately describing the genes referred to. It is unclear as to what genes are therefore described.

Claims 8, 14-17, 26, 32-35, 43, 60, 67, 83 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the disclosure fails to enable the claimed invention: It is observed that the claims are directed to methods of administration of bone marrow comprising proteins that enhance the production of angiogenic growth factors and/or promote blood vessel formation, solely by prophetic consideration. A number of factors need to be considered for in vivo treatments such as concentration, efficacy and composition comprising the protein in question, due to the unpredictability in the art of protein therapy as it was at the time of filing of the instant application. Therefore, in vivo treatments directed to methods wherein bone marrow comprising any and all proteins are not enabled, in the instant disclosure.

Claims 10, 11, 14-17, 28, 29, 32-35, 45, 46, 49, 62, 63, 66, 67, 68, 79, 80, 83, 85, 86, 91, 92 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the disclosure fails to enable the claimed invention: It is observed that the claims are directed to methods of administration of bone marrow comprising genes that are expected to enhance the production of angiogenic growth factors and/or promote blood vessel formation, solely by prophetic consideration. A number of factors need to be considered for in vivo treatments comprising the administration of a gene, or DNA or any vector carrying a gene of interest, due to the unpredictability in the art of gene therapy as of the date of filing of the instant application. Therefore, in vivo treatments directed to methods wherein bone marrow comprising any and all genes or vectors comprising genes of interest are not enabled, in the instant disclosure.

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 48/00	A1	(11) International Publication Number: WO 00/57922 (43) International Publication Date: 5 October 2000 (05.10.00)
(21) International Application Number: PCT/US00/08353 (22) International Filing Date: 30 March 2000 (30.03.00) (30) Priority Data: 60/126,800 30 March 1999 (30.03.99) US 60/138,379 9 June 1999 (09.06.99) US (71)(72) Applicants and Inventors: KORNOWSKI, Ran [US/US]; 12218 Tildenwood Drive, Rockville, MD 20852 (US). FUCHS, Shmuel [US/US]; 267 Rollins Avenue, Rockville, MD 20852 (US). EPSTEIN, Stephen, E. [US/US]; 11700 Danville Drive, Rockville, MD 20852 (US). LEON, Martin, B. [US/US]; 8822 Burdette Road, Bethesda, MD 20817 (US). (74) Agents: DIPPERT, William, H. et al.; Cowan, Liebowitz & Latman, P.C., 1133 Avenue of the Americas, New York, NY 10036-6799 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: INTRAMYOCARDIAL INJECTION OF AUTOLOGOUS BONE MARROW		
(57) Abstract A method of treating cardiac or myocardial conditions comprises the administration of an effective amount of autologous bone marrow. The bone marrow may optionally be stimulated and/or administered in combination with a pharmaceutical drug, protein, gene or other factor or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation or migration or blood vessel formation.		

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EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/08353

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K48/00.

US CL : 424/93.7.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/93.1, 424/93.7.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Medline, Embase, Sciserach, WEST, CAPLus.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	BRUGGER, et al. Ex Vivo Manipulation of Hematopoietic Stem and Progenitor Cells. Seminars in Hematology, 2000, Vol. 37, No. 1, pages 42-49.	1-102
Y	FIELDING, et al. Autologous Bone Marrow Transplantation. Current Opinion in Hematology, 1994, Vol. 1, pages 412-417. See page 1.	1-102
Y	VAUGHAN, et al. Incorporating Bone Marrow Transplantation Into NCCN Guidelines. Oncology, 1998, Vol. 12, No. 11A, pages 390-392. See page 391.	1-102
Y	SIMNETT, et al. Autologous Stem Cell Transplantation for Malignancy: A Systematic Review of the Literature. Clin Lab Haem, 2000, Vol. 22, pages 61-72.	1-102
Y,P	BLUME, et al. A Review of Autologous Hematopoietic Cell Transplantation. Biology of Blood and Marrow Transplantation, 2000, Vol. 6, pages 1-12.	1-102
X,P	NOISHIKI, et al. Angiogenic Growth Factor Release System for In vivo Tissue Engineering: A Trial of Bone Marrow Transplantation into Ischemic Myocardium. J Artif Organs, 1999, Vol. 2, pages 85-91.	1-102
X	KANJ, et al. Myocardial Ischemia Associated With High-dose Carmustine Infusion. Cancer, 1991, Vol. 68, No. 9, pages 1910-1912.	1-102



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

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Date of the actual completion of the international search

8 June 2000

Date of mailing of the international search report

12 JUL 2000

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

David Nikodem

Telephone No. (703) 308-1123

INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DINI, et al. Peripheral Blood Stem Cell Collection from G-CSF-stimulated Unrelated Donors for Second Transplant. Bone Marrow Transplantation, 1998, Vol. 22, No. Suppl 5, pagesS41-S45.	1-102